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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/642,405	08/21/2000	Michael P. Neerer	20413Y	8029
7590	09/22/2004			
Alyria A. Finnegan c/o Merck & Co., Inc. Patent Dept. Ry60-30 P.O. Box 2000 Rahway, NJ 07065-0907			EXAMINER LI, QIAN JANICE	
			ART UNIT 1632	PAPER NUMBER
			DATE MAILED: 09/22/2004	

Please find below and/or attached an Office communication concerning this application or proceeding.

<b>Office Action Summary</b>	<b>Application No.</b>	<b>Applicant(s)</b>	
	09/642,405	NEEPER ET AL.	
	<b>Examiner</b> Q. Janice Li	<b>Art Unit</b> 1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --  
**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM  
 THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) Responsive to communication(s) filed on 14 June 2004.
- 2a) This action is **FINAL**.                  2b) This action is non-final.
- 3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) Claim(s) 1-4,6,7,10,11,15,17-23 and 31 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) Claim(s) 11,15 and 18 is/are allowed.
- 6) Claim(s) 1-4,6,10,17,19-23 and 31 is/are rejected.
- 7) Claim(s) 7 is/are objected to.
- 8) Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) The specification is objected to by the Examiner.
- 10) The drawing(s) filed on 21 August 2000 is/are: a) accepted or b) objected to by the Examiner.  
 Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) The proposed drawing correction filed on \_\_\_\_\_ is: a) approved b) disapproved by the Examiner.  
 If approved, corrected drawings are required in reply to this Office action.
- 12) The oath or declaration is objected to by the Examiner.

**Priority under 35 U.S.C. §§ 119 and 120**

- 13) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) All b) Some \* c) None of:
1. Certified copies of the priority documents have been received.
2. Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.
- 14) Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) The translation of the foreign language provisional application has been received.
- 15) Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

**Attachment(s)**

- 1) Notice of References Cited (PTO-892)
- 2) Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) Information Disclosure Statement(s) (PTO-1449) Paper No(s) 6/14/04.
- 4) Interview Summary (PTO-413) Paper No(s). \_\_\_\_\_.
- 5) Notice of Informal Patent Application (PTO-152)
- 6) Other: \_\_\_\_\_.

## **DETAILED ACTION**

The amendment, response, and declaration filed June 14, 2004 have been entered. Claim 30 has been cancelled. Claims 1-4, 6, 7, 10, 11, 15, 17, 18, 20, 22 have been amended. Claim 31 is newly submitted. Claims 1-4, 6, 7, 10, 11, 15, 17-23, and 31 are pending in the application and under current examination.

Unless otherwise indicated, previous rejections that have been rendered moot in view of the amendment, declaration, and the new ground of rejection will not be reiterated.

### ***Claim Objections***

Claim 3 is objected to because the claim number from which claim 3 depends from is missing.

Claim 7 is objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Claim 23 stand objected to because a comma should be inserted before the "wherein" phrases.

### ***Claim Rejections - 35 USC § 112***

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the

art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Previous rejection under 35 U.S.C. 112, first paragraph is reinstated (see details on pages 6-9 of the Office action mailed June 5, 2002) for reasons of record and following.

Claims 1-4, 6, 10, 17, 19-23, and 30 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for making and using a synthetic polynucleotide comprises SEQ ID Nos: 1, 2, 3, or 4, which are codons optimized for expression in human 293 cells, does not reasonably provide enablement for making and using a synthetic polynucleotide comprising unspecified codon that are optimized for expression in any cell of a human host. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

The factors to be considered when determining whether the disclosure satisfies the enablement requirements and whether undue experimentation would be required to make and use the claimed invention are summarized in *In re Wands*, (858 F2d 731, 737, 8 USPQ 2d 1400, 1404, (Fed Cir. 1988)). These factors include but are not limited to the nature of the invention, the state of the prior art, the relative skill of those in the art, the predictability of the art, the breadth of the claims, and amount of direction provided. The factors most relevant to this rejection are the scope of the claims relative to the state of the art and the levels of the skilled in the art, and whether sufficient amount of direction or guidance are provided in the specification to enable one of skill in the art to practice the claimed invention.

Given the broadest reasonable interpretation, these claims encompass a genus of synthetic polynucleotides comprising codons for numerous HPV16 proteins such as recited in claim 2, wherein the codons have been optimized for expression in human cells. The specification provides general teaching for means of obtaining such codons (e.g. Specification, page 7), and theoretically the claimed genus of codons could be made by the teaching of the specification. However, in the response and Declaration of William L. McClements, the co-applicant and a skilled artisan cited numerous art of record and spoke from his own experience, stated that at the time of the invention, codon-optimization is not always successful at *increasing* expression of a particular gene, and successful condo-optimization of one gene is not predictive of the future success of a different gene. "We did not have an expectation of success" (point 5 of the Declaration). The declaration exemplified such opinion by a showing that the gene expression did not improve for the "optimized" HSV2 codon, and gene expression even decreased upon codon-optimization for tuberculosis. The declaration further indicated that the codon-optimization is not always successful at producing increased gene expression in a cell type of interest, and is not predictable of future success from one gene to the other (point 6 of the declaration). The declaration additionally indicated the presence of inhibitory sequences is unique for different genes (point 7 of the declaration). In view of such, what is successful for increased gene expression of HPV16 L1 gene is not predictable of the future success for HPV16 L2 gene, and likewise what is successful in 293 cells is not predictive of other human cell types.

The merit of the declaration is consistent with the opinion of the Office in the previously issued rejection, which indicated that determination of the effects of particular codon modifications is not predictable until they are actually made and used, hence resulting in a trial and error situation.

Reinforced by the content of the response and declaration, it is reasonably concluded the specification fails to provide adequate support for the broadly claimed inventions because the claims encompass numerous proteins/genes of HPV16, and for each protein/gene, the claims encompass numerous codons that could be optimized for expression in various human cells. Although the specification provided one sequence for each of the L1, E1, E2, and E7 of HPV16, which have proven to be optimized for expression in certain human cells, it is not predictable from the disclosed sequences to the genus of sequences encompassing numerous options for each and every HPV16 proteins to be increasingly expressed in various human cells.

Therefore, in view of the state of the art as illustrated in the declaration, the lack of predictability of the art, and the breadth of the claims, one skill in the art could not practice the invention without undue experimentation as it is broadly claimed.

### ***Conclusion***

Claims 11, 15, and 18 are allowable.

**THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to **Q. Janice Li** whose telephone number is 571-272-0730. The examiner can normally be reached on 9:30 am - 7 p.m., Monday through Friday, except every other Wednesday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, **Amy Nelson** can be reached on 571-272-0804. The fax numbers for the organization where this application or proceeding is assigned are **703-872-9306**.

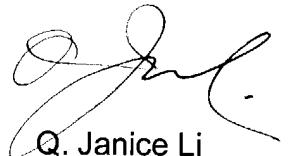
Any inquiry of formal matters can be directed to the patent analyst, **Dianiece Jacobs**, whose telephone number is (571) 272-0532.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance.

Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.



Q. Janice Li  
Primary Examiner  
Art Unit 1632

  
September 17, 2004